REMARKS

The Office Action and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 1-6, 12-18, 20, 25, 27, and 30 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 6, 20 and 27 have been objected to by the examiner. The examiner's suggestion is adopted, and the claims are appropriately amended, thereby obviating the objections.

Claims 1-6, 12-18, 20, 25, 27, and 30 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite. This rejection is obviated by the amendments to the claims, which adopt the examiner's suggestions.

Claims 1-4, 12, 14-16, 18, 20, 25, 27, and 30 have been rejected under 35 U.S.C. §103(a) as being unpatentable over the Invitrogen 1997 product catalog. The examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to:

(1) make an expression vector wherein said vector comprises a nucleotide sequence encoding an IgG (κ) or a trypsin secretory signal peptide, a nucleotide sequence encoding a polyhistidine tag, a nucleotide sequence encoding a polypeptide comprising amino acids 36-40 of SEQ ID NO: 19 (DDDDK; enterokinase cleavage site), and a cloning site into which a

polynucleotide encoding a target protein is inserted,

(2) make an expression vector as described in (1) above, further comprising a nucleotide sequence encoding an antibody recognition epitope,

(3) transform a host cell with the vectors described in (1) or (2), and

(4) make a recombinant fusion protein comprising a target protein by cultivating the host cells of (3), in view of the teachings of the Invitrogen 1997 Catalog.

The examiner further asserts that a person of ordinary skill in the art is motivated to modify the pRSET vector such that the IgG(κ) secretion signal and the c-myc epitope of the pSecTag vector are added for the benefit of creating an expression vector which allows for secretion of the desired protein and a purification tag. The examiner further takes the position that a person of ordinary skill in the art is motivated to add the pRSET's polynucleotide encoding the enterokinase cleavage site to the pSecTag vector next to the His6 tag for the benefit of being able to cleave the His6 tag from the target protein after purification and, additionally, that a person of ordinary skill in the art is motivated to place the polynucleotide encoding the His6 tag prior to the cloning site as

the His6 tag may affect the folding/activity of the protein of interest depending on whether the His6 tag is at the C or N terminus. This rejection is respectfully traversed.

As pointed out by the examiner, a secretion signal peptide, a tag sequence, a cleavable nucleic acid sequence, and a cloning site were the sequences or the sites which were known at the time the present invention was made. The 1997 Invitrogen catalog discloses a vector which can express a protein by combining these sequences on the vector.

By contrast, the vector of the present invention contains 3'-downstream of a secretion signal nucleic acid sequence, a Tag nucleic acid sequence, a cleavable nucleic acid sequence, and a cloning site into which a nucleic acid sequence encoding a protein of interest can be inserted, in this particular order. A protein expressed using the vector of the present invention includes essential elements of a secretion signal, Tag, a cleavable sequence, and a protein of interest from the a N-terminal side, and a secreted protein, from which a secretion signal was removed, which includes the remaining portion of the essential elements of Tag, a cleavable sequence and a protein of interest from the N-terminal side. By using an enzyme recognizing a cleavable sequence for this protein, since the protein can be cleaved at a cleavable sequence, a recombinant

protein that is finally obtained has no extra amino acid added thereto (at least not on the C-side of a protein of interest).

When the Invitrogen vector and the vector of the present invention are compared, the vector (pRSET A, B, C) described on 37 page of the cited reference lacks a nucleic acid sequence encoding a secretion signal. Although the cited reference on page 46 discloses a vector containing a nucleic acid sequence encoding a secretion signal, an extra amino acid such as for the myc-epitope and His tag is added to the expressed protein. Thus, the Invitrogen catalog does not suggest at all the feature possessed by the present invention in which the protein of interest does not have an added extra amino acid.

From the above discussion, while the components of the vector of the present invention were known, the new advantageous effects of an expressed protein containing these components in a particular order, such as being secreted outside a host cell due to a secretion signal, where the secreted protein is easily purified with a tag sequence and where, by enzyme-treating a cleavable sequence after purification, a tag sequence and a cleavable sequence are separated and a protein of interest with no extra amino acid sequence added can be obtained, are not disclosed, taught or suggested in the cited reference.

At the time the present invention was made, no vector having all of these characteristics simultaneously was disclosed

or suggested in the prior art. Thus, the presently claimed vector possesses superior properties and advantages over those of the prior art vectors discussed above. Moreover, when even one place in the order of essential components in the presently claimed vector is different, the vector of the present invention cannot possess the aforementioned effects or advantages. Considering the superior effects and advantages over the prior art afforded by the vector of the present invention, the 1997 Invitrogen catalog cannot make obvious the presently claimed invention.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By _____
Allen C. Yun
Registration No. 37,971

ACY:pp
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\A\Aoyb\Uemura8\PTO\AMD OA 11-4-03.doc